

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property  
Organization  
International Bureau



553 307

(43) International Publication Date  
28 October 2004 (28.10.2004)

PCT

(10) International Publication Number  
WO 2004/092707 A2

(51) International Patent Classification<sup>7</sup>: G01N  
(21) International Application Number: PCT/US2004/011426  
(22) International Filing Date: 14 April 2004 (14.04.2004)  
(25) Filing Language: English  
(26) Publication Language: English

(30) Priority Data: 60/462,997 14 April 2003 (14.04.2003) US

(71) Applicant (for all designated States except US): WATERS INVESTMENTS LIMITED [US/US]; 109 Lukens Drive, New Castle, DE 19720 (US).

(72) Inventors; and

(75) Inventors/Applicants (for US only): GEBLER, John, C. [US/US]; 160 Ash Street, Hopkinton, MA 01748 (US). LEE, Peter, J., J. [US/US]; 38 Byard Lane, Westborough, MA 01757 (US). CHEN, Weibin [US/US]; 51 Maryilyn Street, Holliston, MA 01746 (US).

(74) Agent: JANIUK, Anthony, J.; Waters Corporation, 34 Maple Street, Milford, MA 01757 (US).

(81) Designated States (unless otherwise indicated, for every kind of national protection available): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.

(84) Designated States (unless otherwise indicated, for every kind of regional protection available): ARIPO (BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

**Published:**

— without international search report and to be republished upon receipt of that report

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: AROMATIC PHOSPHONIUM SALTS AND THEIR USE AS LABELING REAGENTS MASS SPECTROMETRY ANALYSIS

(57) Abstract: This invention relates to methods and reagents for the assay, detection, quantification, location, or analysis of each of a plurality of substances of interest ("analytes") in a sample in which each substance is labeled with a cationic triarylphosphonium group. The present invention also provides MALDI mass spectrometry techniques in which the analysis of samples containing low molecule weight analytes is not obscured by matrix components. The invention also provides labeling reagents for use in labeling analytes prior to MS analysis in which the labeled analytes have a molecular weight above the useful detection threshold of MALDI techniques. In some aspects, the invention provides methods of quantitative MS analysis of components of a sample. Methods of the present invention include sensitive techniques for desorption/ionization of molecules at the picomole, femtomole, and attomole amounts. Another benefit of the present invention is that measurement of m/z values is not complicated by the low-mass interference that a matrix normally offers, and therefore the invention provides methods of MALDI MS analysis of low molecular weight samples as well as mixtures of high and low molecular weight samples.



WO 2004/092707 A2